REMARKS

The following remarks are responsive to the Office Action set forth above. Claims 1-27 were originally presented, and claims 28-30 were added by a Preliminary Amendment dated April 2, 2002. Claims 1-4 are cancelled, and claims 5, 12, and 28 are presently amended. Claims 31-34 are added. Claims 5-34 are pending after entry of this Amendment.

Amendment to claims 5, 12, and 28, and the new claims, are fully supported by the specification. No new matter is introduced into the application by the claim amendments and the new claims.

In particular, the recitation of mesh size is supported in the specification at page 7, lines 3-6, and in original claim 2 (now cancelled). The recitation of a continuous coating is supported in the specification at page 7, lines 12-15 and page 8, lines 10-11. New claims 31-34 are supported in the specification at page 11, lines 7-9.

The present invention, in the embodiment claimed by claims 5-11, encompasses an extended-release tablet comprising a plurality of granules consisting of potassium chloride crystals between about 20 to about 60 mesh, and a continuous coating on the crystals, the coating consisting of a thermoplastic cellulose ether.

The invention also includes, as recited in claims 12-16, a dosage unit in tablet form comprising granules having an internal core of potassium chloride between about 20 and about 60 mesh, and a continuous external coating of ethylcellulose, wherein the granules are essentially free of surfactants or processing aids and agents.

Another embodiment of the invention, recited in claims 17-26, provides fluidized-bed methods for making granules of potassium chloride coated by ethylcellulose. The methods include the step of spraying potassium chloride crystals with a mixture consisting of ethylcellulose, alcohol and water to coat the crystals.

The invention, as recited in claim 27, further encompasses a method for customizing a patient's supplemental potassium dosage regimen by providing dosage units having various potencies, and administering the potencies in suitable combination to meet the patient's supplemental potassium requirements.

Another embodiment of the invention includes, as recited in claims 28-30, a pharmaceutical dosage unit in tablet form comprising a plurality of granules having an internal core of potassium chloride between about 20 to about 60 mesh and a continuous external extended release coating, wherein the dosage unit contains 15 mEq potassium.

Also included within the scope of the invention, as recited in new claims 31-34, is a process to produce a pharmaceutical dosage unit in tablet form, the dosage unit comprising ethylcellulose-coated potassium chloride granules. The method includes the steps of forming a fluidized-bed of potassium chloride crystals, and spraying the potassium chloride crystals with a mixture consisting of ethylcellulose, alcohol and water to coat the crystals. A plurality of ethylcellulose-coated granules is subsequently compressed into a tablet.

Claim Rejections – 35 U.S.C. § 102

The Examiner rejected claims 1, 3, 5 and 8 under 35 U.S.C. § 102(b) as anticipated by U.S. Patent 3,873,588 to Osawa, *et al.* ("Osawa"). Claims 1 and 3 are cancelled, and claim 5 is amended. With respect to claims 5 and 8, the rejection is traversed.

It is respectfully submitted that in the Office action the Examiner has mischaracterized claim 5 as drawn to a tablet containing granules that *comprise* potassium chloride and a thermoplastic cellulose ether. In fact, claim 5 is directed to an extended-release tablet comprising a plurality of granules *consisting of* potassium chloride crystals between about 20 to about 60 mesh, and a continuous coating on the crystals, the coating consisting of thermoplastic cellulose ether. Claim 8 depends from claim 5, and specifies that the thermoplastic cellulose ether is ethylcellulose.

Osawa reports an orally administrable pharmaceutical iron preparation having gradual release activity, the preparation comprising an iron salt of a carboxyl group-containing water-soluble polymer. Although the preparations of Osawa may include potassium chloride and a cellulose ether, Osawa does not provide a granule *consisting of* potassium chloride crystals and a thermoplastic cellulose ether. "The transitional phrase 'consisting of' excludes any element, step, or ingredient not specified in the claim." M.P.E.P. § 2111.03. Applicants respectfully request that the rejection be withdrawn. Claim 8 depends from claim 5, and recites additional features. Claim 8 is therefore not anticipated for at least the same reasons.

The Examiner has also rejected claims 1, 3, and 5 under § 102(b) as anticipated by U.S. Patent 4,259,315 to Lippman, *et al.* ("Lippman"). Claims 1 and 3 are cancelled, and claim 5 is amended. With respect to claim 5, the rejection is respectfully traversed.

Lippman reports pharmaceutical compositions comprising gelatin capsules containing a mixture comprising a controlled-release form of microencapsulated potassium salt and hydrophilic surfactant (Abstract). The microencapsulated potassium salt, or "microcapsules," is described at col. 3 line 53 to col. 4 line 28 of Lippman.

The present claim 5 is directed to an extended-release tablet comprising a plurality of potassium chloride granules consisting of crystals between about 20 to about 60 mesh, and a continuous coating on the crystals, the coating consisting of thermoplastic cellulose ether. Lippman reports only capsules, and does not provide a pharmaceutical dosage unit in tablet form. Nor does Lippman provide methods for tabletting that would be suitable for the reported microcapsules. Lippman therefore cannot anticipate claim 5, and the rejection should be withdrawn.

The Examiner has rejected claims 1-5 under § 102(b) as anticipated by U.S. Patent 5,397,574 to Chen ("Chen"). Claims 1-4 are cancelled. With respect to claim 5, the rejection is respectfully traversed.

Chen reports a pharmaceutical composition for oral administration in tablet or capsule form comprising micropellets of a potassium salt. The micropellets are coated with a low-viscosity ethylcellulose in combination with a plasticizer such as triacetin (Abstract). The plasticizer was reported to enable use of a low-viscosity ethylcellulose while reducing frangibility of the resulting coating (col. 2, lines 45-47). Each embodiment of Chen requires a plasticizer; see, e.g., Example 1 and claims 1, 8, and 14.

Chen does not, therefore, provide a feature recited in present claim 5, namely a granule *consisting of* potassium chloride crystals and a thermoplastic cellulose ether. Applicants respectfully request that the rejection be withdrawn.

The Examiner has rejected claims 1-5, 8, 10, 11 and 27 under § 102(b) as anticipated by U.S. Patent 4,863,743 to Hsiao, *et al.* ("Hsiao"). Claims 1-4 are cancelled. Claim 5 is presently amended. With respect to claims 5, 8, 10, 11 and 27, the rejection is respectfully traversed.

Hsiao reports a controlled-release potassium chloride tablet comprising potassium chloride crystals coated with a polymeric coating comprising ethylcellulose and either hydroxypropylcellulose or polyethylene glycol (col. 4, lines 4-21 and lines 32-33). Hsiao does not, therefore, provide a feature recited in present claims 5, 8, 10, and 11, namely a granule *consisting of* potassium chloride crystals between about 20 to about 60 mesh, and a continuous coating on the crystals, the coating *consisting of* a thermoplastic cellulose ether. Applicants respectfully request that the rejection be withdrawn.

The present claim 27 is directed to a method for customizing a patient's supplemental potassium dosage regimen, and recites the step of providing pharmaceutical dosage units containing about 10 mEq potassium, 15 mEq potassium, and 20 mEq potassium. Hsiao does not provide a dosage unit containing about 15 mEq potassium. At col. 5, lines 41 to 55, Hsiao refers to a tablet providing 20 mEq potassium, and states that "With the formulation provided by the present invention the tablet will include 20 mEq so that the recommended effective amount of potassium per single dose would not be altered."

It is respectfully submitted that Hsiao does not anticipate the method of claim 27, since Hsiao does not provide pharmaceutical dosage units containing about 10 mEq potassium, 15 mEq potassium, and 20 mEq potassium. Withdrawal of the rejection is requested.

Claim Rejections – 35 U.S.C. § 103

The Examiner has rejected claims 1-16 and 27-30 as unpatentably obvious over Hsiao. Claims 1-4 are cancelled. With respect to claims 5-16 and 27-30, the rejection is traversed.

Claim 5 is directed to an extended-release tablet comprising a plurality of granules *consisting of* potassium chloride crystals between about 20 to about 60 mesh, and a continuous coating on the crystals, the coating *consisting of* a thermoplastic cellulose ether. Claims 6-11 depend directly or indirectly from claim 5, and recite additional features.

Hsiao reports a controlled-release potassium chloride tablet comprising potassium chloride crystals coated with a polymeric coating comprising ethylcellulose and either

hydroxypropylcellulose or polyethylene glycol (col. 4, lines 4-21 and lines 32-33). The present invention as recited in claim 5 includes a coating consisting of a thermoplastic cellulose ether. Hsiao does not, therefore, provide a feature recited in present claim 5, namely a granule *consisting of* potassium chloride crystals between about 20 to about 60 mesh, and a continuous coating on the crystals, the coating *consisting of* a thermoplastic cellulose ether.

Furthermore, Hsiao neither teaches nor suggests that a coating consisting of thermoplastic cellulose ether is suitable for making a controlled-release potassium chloride tablet. Hsiao provides no motivation to eliminate the hydroxypropylcellulose or polyethylene glycol that is included in the reported coatings. Claim 5 therefore cannot be considered obvious over Hsiao. Claims 6-11 depend directly or indirectly from claim 5, and recite additional features. Claims 6-11 are therefore unobvious over the cited reference for at least the same reasons.

Claim 12 is directed to a pharmaceutical dosage unit in tablet form comprising a plurality of granules having an internal core of potassium chloride between about 20 to about 60 mesh and a continuous external coating consisting of ethylcellulose, wherein the granules are essentially free of surfactants or processing aids and agents. Claims 13-16 depend from claim 12 and recite additional features.

Again, Hsiao neither teaches nor suggests that a coating consisting of ethylcellulose is suitable for making a controlled-release potassium chloride tablet. Hsiao provides no motivation to eliminate the hydroxypropylcellulose or polyethylene glycol that is included in the reported coatings. Claim 12 therefore cannot be considered obvious over Hsiao. Claims 13-16 depend directly or indirectly from claim 12, and recite additional features. Claims 13-16 are therefore unobvious over the cited reference for at least the same reasons.

Claim 27 is directed to a method for customizing a patient's supplemental potassium dosage regimen. Claim 27 recites, as one step in the method, the step of providing pharmaceutical dosage units containing about 10 mEq potassium, 15 mEq potassium, and 20 mEq potassium.

Hsiao does not report a dosage unit containing about 15 mEq potassium. At col. 5, lines 41 to 51, Hsiao discusses daily dosages and available dosage units:

> The recommended dose in most patients is 40 mEq per day in divided doses. In accordance with currently approved labeling 20 mEq, or 2 doses having a size of 10 mEq should be taken twice daily in order to obtain a daily dose of 40 mEq. With the formulation provided by the present invention the tablet will include 20 mEq so that the recommended effective amount of potassium per single dose would not be altered. The daily dose would be achieved with one tablet twice daily thus facilitating compliance due to less individual units per dose.

Although the recommended dose for most patients is 40 mEq per day in a divided dose, as indicated by the section quoted above, a different dosage may be prescribed by a doctor depending on the supplemental need of the patient. For instance, a dosage of 30 mEq may be adequate for a patient in some circumstances. The quotation from Hsiao given above indicates that it is preferred that a patient's supplemental potassium be administered twice-daily in symmetrically divided dose. The quotation also indicates the need to encourage compliance by a patient, by providing dosage forms that are convenient to administer.

The quotation from Hsiao given above also demonstrates a lack of appreciation in the art that certain prescribed dosages, such as 30 mEq, would be difficult to administer in a symmetrically divided dose when the only available dosage units contain the conventional 10 mEq or 20 mEq. Furthermore, it should be recognized that it is disfavored to require physical splitting of a dosage unit (such as cutting a 10 mEq dosage unit into two equal halves) to achieve a proper dosage. If a tablet is split, it is likely that the coating that enables controlled-release properties of the active ingredient would be damaged, and the controlled-release feature compromised.

By providing a dosage unit having 15 mEq potassium, the present invention, in contrast to the prior art cited by the Examiner, permits a daily dosage of 30 mEq to be administered in symmetrically divided dosages. Using the dosage units indicated in Hsiao, a daily dosage of 30 mEq would have to be administered as either a one-time dosage of 20 mEq with a separate dosage of 10 mEq, or as a thrice-daily administration of 10 mEq. The methods of the present invention, as claimed in claim 27, overcome this limitation.

The method claimed in claim 27 also permits other daily dosages, such as 25 mEq, 35 mEq, or 45 mEq to be prescribed and administered. Using only the conventional dosage units containing either 10 mEq or 20 mEq, it is not possible to achieve daily dosages of 25 mEq, 35 mEq, or 45 mEq without difficulty. The method therefore provides much greater flexibility to a doctor in prescribing an appropriate supplemental potassium dosage.

Hsiao neither teaches nor suggests providing a 15 mEq dosage unit in addition to the conventional 10 mEq and 20 mEq sizes. Therefore, Hsiao cannot be considered to make obvious the method of the present invention as claimed in claim 27. Withdrawal of the rejection is requested.

Claim 28 is directed to a pharmaceutical dosage unit in tablet form comprising a plurality of granules having an internal core of potassium chloride between about 20 to about 60 mesh and a continuous external extended release coating, wherein the dosage unit contains 15 mEq potassium. Claims 29 and 30 depend from claim 28 and recite additional features.

As discussed above, Hsiao neither teaches nor suggests providing a 15 mEq dosage unit. Therefore, Hsiao cannot be considered to make obvious the present invention as claimed in claim 28. Withdrawal of the rejection is requested. Claims 29 and 30 depend from claim 28 and recite additional features. Claims 29 and 30 are therefore unobvious over the cited reference for at least the same reasons.

The Examiner has rejected claims 17-26 as unpatentably obvious over Hsiao in view of U.S. Patent 4,748,023 to Tamás, *et al.* ("Tamás"). Claims 17-26 are directed to fluidized-bed processes for producing ethylcellulose-coated potassium chloride granules. The processes, as recited in independent claims 17 and 22, include the step of spraying a fluidized bed of potassium chloride crystals with a mixture *consisting of* ethylcellulose, alcohol and water.

The Examiner states that Hsiao reports a tablet comprising granules of potassium chloride coated with ethyl cellulose. The Examiner states that the granules of Hsiao are coated in a fluidized bed with a solvent solution including methyl alcohol and distilled water, with the solvent subsequently removed during a drying step to yield granules coated with ethyl cellulose.

Hsiao reports a controlled-release potassium chloride tablet including potassium chloride crystals coated with a polymeric coating comprising ethylcellulose *and* either hydroxypropylcellulose or polyethylene glycol (col. 4, lines 4-21). The polymeric coating contains predominantly ethylcellulose, with a ratio of about 3.0 to about 30 parts ethylcellulose by weight per one part hydroxypropylcellulose or polyethylene glycol (col. 4, lines 10-13).

As demonstrated in the Examples of Hsiao, potassium chloride crystals may be coated using a fluidized bed process. The process of Hsiao utilizes a co-solvent system consisting of chloroform and methanol in a 4:1 ratio (see col. 6, lines 14-16; and col. 6, lines 50-52). A mixture of polymers is dissolved in the chloroform/methanol co-solvent system. In Example 1, the mixture of polymers includes ethylcellulose and polyethylene glycol (col. 6, lines 11-13). In Example 2, the mixture of polymers includes ethylcellulose and hydroxypropylcellulose (col. 6, lines 47-52).

The Examiner states that Tamás demonstrates a fluidized bed coating process of making potassium chloride granules, at a temperature of 20° C. It is respectfully submitted by the Applicants that Tamás does not report fluidized bed processes for coating pharmaceutically active ingredients.

Tamás states at col. 4, lines 23-37 that microencapsulation may be carried out with the aid of any suitable microencapsulation process capable of forming a uniform continuous coating on the surface of the crystal particles of the active ingredient. However, fluidized-bed processing is not explicitly discussed. Rather, Tamás refers to methods for coating with ethylcellulose, such as a process using cyclohexane as a medium, as reported in U.S. Patent 3,531,418. The coating methods reported in the Examples of Tamás include dissolving an active ingredient and a coating polymer in a large quantity of cyclohexane. See Examples 1 and 2 of Tamás. No suitable parameters for achieving a similar coating by means of a fluidized-bed process are provided by Tamás.

Neither Hsiao nor Tamás, nor the combination of Hsiao and Tamás, therefore teaches or suggests the step of spraying a fluidized bed of potassium chloride crystals with a mixture *consisting of* ethylcellulose, alcohol and water.

The present invention, on the other hand, reports a method by which potassium chloride crystals may be coated using a solvent system consisting of alcohol and water. Nowhere in Hsiao is the use of water in a solvent system for a fluidized-bed coating process taught or suggested. Tamás does not report fluidized-bed coating processes, nor does Tamás report a solvent system consisting of alcohol and water used in a coating process for coating potassium chloride crystals. The combination of Hsiao and Tamás therefore does not teach or suggest the use of a solvent system consisting of alcohol and water in a fluidized-bed coating process.

Furthermore, the fluidized-bed processes reported by Hsiao yield a polymeric coating comprising ethylcellulose and either hydroxypropylcellulose or polyethylene glycol. Hsiao does not provide the step of spraying a fluidized bed of potassium chloride crystals with a mixture *consisting of* ethylcellulose, alcohol and water, as recited in the present claims. As stated above, Tamás does not report fluidized-bed coating processes, and cannot provide the recited step. The combination of Hsiao and Tamás therefore does not teach or suggest the step of spraying a fluidized bed of potassium chloride crystals with a mixture *consisting of* ethylcellulose, alcohol and water.

Furthermore, neither Hsiao nor Tamás, nor the combination of Hsiao and Tamás, teaches or suggests a method for producing ethylcellulose-coated potassium chloride granules by a fluidized-bed process. The present claims 17 and 22 are directed to a process for producing ethylcellulose-coated potassium chloride granules, as recited in the preamble of each. The step of spraying a fluidized bed of potassium chloride crystals with a mixture *consisting of* ethylcellulose, alcohol and water, followed by the step of drying the crystals to remove the water and the alcohol, provides ethylcellulose-coated potassium chloride granules. The fluidized-bed processes reported by Hsiao, in contrast, yield a polymeric coating comprising ethylcellulose and either hydroxypropylcellulose or polyethylene glycol. Tamás does not report fluidized-bed coating processes.

The combination of Hsiao and Tamás cannot render the claimed invention, as claimed in claims 17 and 22, obvious. Withdrawal of the rejection is requested. Claims 18-21 and 23-26 are unobvious over the cited combination, for at least the same reasons.

C nclusion

All pending claims are now in condition for allowance. A notice to that effect is respectfully requested.

Respectfully Submitted,

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